

201-14999A

Carbonothioic dihydrazide

CAS # 2231-57-4

HPV Test plan

Bayer CropScience LP

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Executive Summary

Bayer CropScience LP (Bayer) hereby submits for review and public comment their test plan for Carbonothioic dihydrazide (CAS# 2231-57-4) under the Environmental Protection Agency's High Production Volume (HPV) Chemical Challenge Program.

<u>IUPAC Name</u>	<u>Common Name</u>	<u>Abbreviation</u>	<u>CAS#</u>
1,3-diamino-2-thiourea	thiocarbohydrazide	TCH	2231-57-4

Thiocarbohydrazide (TCH) is used as an intermediate in the production of an agricultural herbicide and, in limited quantities, as an intermediate in the production of a "fine" chemical.

In consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals, Bayer has conducted a thorough literature search for all available data, published and unpublished. It has also performed an analysis of the adequacy of the existing data. Existing data indicates that this chemical is of low-moderate concern for aquatic toxicity, low concern as Persistent Organic Pollutants (POP), low concern for skin irritation, and a moderate to high concern for mammalian toxicity. In a separate submission (confidential business information), Bayer has explained in detail that this substance is a closed-system intermediate and therefore a reduced data set is required. To fulfill the SIDS data set, an acute Algal Growth Inhibition study (OECD 201), an *in vivo* Mouse Micronucleus study (OECD 474), and a Teratogenicity study (OECD 414) on TCH is proposed for purposes of the HPV Program.

Closed System Intermediate Chemical Status

A separate document is being submitted to EPA to describe the process, sites, and transport of TCH to explain “closed-system” intermediate status. This information is considered Confidential Business Information and therefore is not available to the public in this document.

Data Review

Physicochemical properties:

The properties of TCH can be found in handbooks and various endpoints were calculated with EPIWin Modeling Program. TCH is solid at ambient temperatures and will decompose before melting. The calculated octanol/water partition coefficient is -2.04 and TCH is very soluble in water. Data is available for all endpoints, no additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Environmental Fate:

Photodegradation was calculated as a half-life of 1.4 hours for TCH. Fugacity modeling demonstrates partitioning to the soil and water compartments. Biodegradation modeling demonstrates that TCH is readily biodegradable. No water stability study has been located, but TCH is handled as a “wet-cake” and is expected to be stable in an aqueous environment. Since analytical monitoring will be done during the aquatic toxicity testing, stability will be confirmed. In the expectation of confirmed stability, no additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Ecotoxicology:

No aquatic studies have been found. EcoSAR modeling give LC₅₀ results of 24.5 mg/l (96 hr fish); 17.95 mg/l (24 hr *Daphnia*); 1.141 mg/l (144 hr Algae) using the EcoSAR chemical class, Hydrazines. In order to limit the use of animals in testing and since TCH appears to be most toxic to Algae, an OECD 201 test is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Mammalian Toxicology:

Toxicity studies in animals show that TCH is of high acute toxicity following oral exposure with a lower magnitude of toxicity observed following dermal or inhalation exposures: oral LD₅₀ = 26.5 mg/kg (female rat); inhalation LC₅₀ 50 mg/m³ (rat); and dermal LD₅₀ > 500 mg/kg (rabbit). (See Table 1 and IUCLID document).

There is an Ames and an Unscheduled DNA Synthesis study on TCH to fill the mutagenicity endpoint. No studies on chromosome aberration were located. Since both *in vitro* studies were positive, an *in vivo* Mouse micronucleus study (OECD 474) on TCH is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

There were no repeated dose, fertility, nor developmental studies found. Since TCH is a "closed-system intermediate", the repeated dose and fertility studies are waived. A "Teratogenicity" study (OECD 414) on TCH is proposed for purposes of the HPV Program. (See Table 1 and IUCLID document).

"Beyond SIDS" Endpoints:

Studies have been performed to investigate skin and eye irritation. TCH was found to be non-irritating to the skin and eyes of rabbits. (See Table 2 and IUCLID document).

Exposure Considerations

Since this chemical is used as a closed-system intermediate, there is limited exposure potential to humans, aquatic organisms and the environment. In addition, TCH has a very low vapor pressure and is handled as a "wet-cake" and does not produce dusting problems. Workers use protective equipment in any situation where accidental exposure is possible. There is no intentional disposal to wastewater system. With controls imposed, exposure is negligible.

Conclusion

Existing data indicate that this chemical is of low-moderate concern for aquatic toxicity, low concern as Persistent Organic Pollutants (POP), low concern for skin irritation, and a moderate to high concern for mammalian toxicity. In a separate submission, Bayer has explained in detail that this substance is a closed-system intermediate and therefore a reduced data set is required. To fulfill the SIDS data set, an acute Algal Growth Inhibition study (OECD 201), an *in vivo* Mouse Micronucleus study (OECD 474), and a Teratogenicity study (OECD 414) on TCH is proposed for purposes of the HPV Program.

Table 1. Available data for TCH (CAS# 2231-57-4)

Endpoint	TCH
Physical-Chemical Data	
Molecular weight	106.15
Physical state	solid
Melting Point	Not applicable Decomposition at 170 °C
Boiling Point	Not applicable Decomposition at 170 °C
Vapor Pressure	< 0.1 hPa
Partition Coefficient (logP _{ow})	-2.04
Water Solubility	Very soluble
Environmental Fate	
Photodegradation	T ½ = 1 hr
Fugacity (distribution)	Air: < 0.01 % Water: 45.3 % Soil: 54.6 % Sediment: < 0.1 %
Biodegradability	Biodegrades fast
Water Stability	No data
Ecotoxicology	
Acute Fish Toxicity 96 hrs LC ₅₀	24.51 mg/l (EcoSAR)
Acute Invertebrate Toxicity 48 hrs LC ₅₀	17.95 mg/l (EcoSAR)
Algal Toxicity 144 hrs LC ₅₀	1.141 mg/l (EcoSAR)
Mammalian Toxicology	
Acute Toxicity	LD ₅₀ = 26.5 mg/kg bw (oral, female rats) LC = 50 mg/m ³ (inhalation, 4 hr, rats) LD ₅₀ > 500 mg/kg bw (dermal, rat)
Mutagenicity	Ames = positive Unscheduled DNA Synthesis = positive
Chromosome Aberration	No data
Repeated Dose Toxicity	No data
Reproductive Toxicity	No data
Developmental Toxicity	No data

* Robust summaries and References can be found in the IUCLID document.

Table 2. “Beyond SIDS” data for TCH

Endpoint	TCH (CAS# 2231-57-4)
Skin Irritation	Not irritating (24 hrs, rabbit)
Eye Irritation	Not irritating (24 hrs, rabbit)

* Robust summaries and References can be found in the IUCLID document.

Table 3. Test Plan for TCH

Endpoint	Data Availability	Acceptable	Planned testing
Physical-Chemical Data			
Melting Point	✓	✓	
Boiling Point	✓	✓	
Vapour Pressure	✓	✓	
Partition Coefficient (logP _{ow})	✓	✓	
Water Solubility	✓	✓	
Environmental Fate			
Photodegradation	✓	✓	
Fugacity	✓	✓	
Biodegradability	✓	✓	
Water Stability			Analytical monitoring in aquatic toxicity study
Ecotoxicology			
Acute Fish Toxicity	✓	✓	
Acute Invertebrate Toxicity	✓	✓	
Algal Toxicity	✓		OECD 201
Mammalian Toxicology			
Acute Toxicity	✓	✓	
Mutagenicity	✓	✓	
Chromosome Aberration			OECD 474
Repeated Dose Toxicity	Not required 'Closed system intermediate'		
Reproductive Toxicity	Not required 'Closed system intermediate'		
Developmental Toxicity			OECD 414

✓ = data available and considered adequate.